

AMENDMENTS TO THE SPECIFICATION

Please amend paragraph [0035] on page 13 as follows:

[0035] It has been reported that ROS enhanced Mac-1 upregulation and anti-oxidants diminished Mac-1-mediated neutrophil accumulation and adhesion following ischemia and reperfusion; (Serrano et al., 1996; Fraticelli A, Serrano CVJ, Bochner BS, Capogrossi MC and Zweier JL, *Biochim Biophys Acta* 1310:251-259,1996). In this study, ROS (O_2^{\ominus} $\text{O}_2^{2\oplus}$ and H_2O_2) production induced by fMLP was diminished by SPRST as well as Tet and Fan (Fig. 4). This indicates that SPRST, Tet, and Fan may act as ROS scavengers through which in turn down-regulate Mac-1 expression and then neutrophil firm adhesion/ transmigration. Our prior studies confirmed that antioxidants (superoxide dismutase and catalase) significantly down regulated ROS production as well as Mac-1 expression and neutrophil adhesion to fibrinogen (Shen YC, et al., *Eur J Pharmacol* 343:79-86,1998). The flow cytometric method used in this study for the measurement of ROS production enabled on-line monitoring of the intracellular accumulation of O_2^{\ominus} $\text{O}_2^{2\oplus}$ and H_2O_2 in neutrophils. We found accumulation of O_2^{\ominus} $\text{O}_2^{2\oplus}$ and H_2O_2 began immediately after stimulation (data not shown). Thus, the rapid accumulation of O_2^{\ominus} $\text{O}_2^{2\oplus}$ and H_2O_2 in response to stimulation and our observation that Mac-1 upregulation could be inhibited by ROS scavengers (Shen et al., 1999) suggests that ROS are early signaling molecules involved in the regulation of neutrophil function. This argument is further intensified by Finkel's observations (Finkel T, *Curr Opin Cell Biol* 10:248-253, 1998) that ROS can act as second messengers in the activation of ligand-stimulated NF- κ B, various protein kinase C (PKC) family members, and mitogen-activated protein kinase (MAPK) as well as tyrosine kinases/phosphatase. Thus, we suggest that ROS could regulate neutrophil functions through second messenger mechanism(s).